



Research Article

SECOND ORDER DERIVATIVE SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF TELMISARTAN AND METOPROLOL IN TABLET DOSAGE FORM

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ABSTRACT

Accurate, precise, rapid and economical method was developed for the estimation of Telmisartan (TELM) and Metoprolol (METO) in bulk and tablet dosage form using second order derivative spectrophotometry. Wavelengths selected for quantitation were 299.5 nm for Telmisartan (zero crossing point of Metoprolol) and 224nm for Metoprolol (zero crossing point of Telmisartan). Linearity was observed in the concentration range of 3-15 μ g/ml for both Telmisartan and Metoprolol. The accuracy and precision were determined and found to comply with ICH guidelines. The proposed method was successfully applied for the simultaneous estimation of both drugs in commercial tablet preparation.

Key words: Telmisartan, Metoprolol, Derivative spectrophotometry, second order, validation

INTRODUCTION

Telmisartan is an angiotensin II receptor antagonist used as an anti-hypertensive drug. Chemically it is 4'-([4-methyl-6-(1-methyl-1H-benzimidazol-2-yl)-2-propyl-1H-benzimidazol-1-yl]methyl)-2-biphenylcarboxylic acid. Metoprolol is a widely used beta-blocker used in the treatment of hypertension. Chemically it is (RS)-1-(Isopropylamino)-3-[4-(2-methoxyethyl) phenoxy] propan-2-ol. Structures of both of the drugs (TELM and METO) are shown in the figure I.^{1,2} Telmisartan and Metoprolol both are official in USP, IP and BP.³⁻⁵

The combination of TELM and METO has been recently introduced in the market for the treatment of moderate to-severe hypertension. Both the drugs are marketed as combined tablet dosage form in the ratio 1:1.25 (TELM: METO)

The analytical techniques reported for the determination of TELM include liquid chromatography (LC), high-performance thin-layer chromatography (HPTLC), spectrophotometry etc. either separately or in combination with other drugs.⁶⁻¹⁰ Several analytical methods that use spectrophotometry, LC and HPTLC have been reported in the literature for the determination of METO in pharmaceutical preparations, either separately or in combination with other drugs.¹¹⁻¹⁴

This paper presents a second order derivative spectroscopic method for the simultaneous determination of TELM and METO in mixtures without prior separation. Also, the utility of the proposed methods for the determination of both drugs in pharmaceutical formulation is demonstrated.

MATERIALS AND METHODS**Apparatus:**

Instrument used was an UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with a pair of 1 cm matched quartz cells. All weighing was done on Shimadzu analytical balance (Model AU-220).

Reagents and chemicals:

Pure drug samples of TELM and METO were obtained from Lupin pharmaceuticals. Methanol LR was used as solvent. Calibrated glass wares were used throughout the work.

Marketed formulation:

Combined tablet formulation (TELSAR BETA TAB) was procured from local market. Each tablet contains 40 mg Telmisartan and 50 mg Metoprolol.

Preparation of standard stock solution:

Accurately weighed quantity of TELM (50 mg) and METO (50 mg) was transferred into two separate 50ml volumetric flasks, dissolved in methanol and diluted to the mark with same solvent. (Stock solutions: 1000 μ g/ml of TELM and 1000 μ g/ml of METO).

Preparation of working standard solution:

100 μ g/ml of TELM solution was prepared by diluting 5.0 ml of stock solution with methanol in 50 ml volumetric flask up to the mark. 100 μ g/ml of METO solution was prepared by diluting 5.0 ml of stock solution with methanol in 50 ml volumetric flask up to the mark.

Procedure for determination of wavelength for measurement:

0.9 ml of working standard solution of TELM (100 μ g/ml) and 0.9 ml of working standard solution of METO (100 μ g/ml) were pipette out into two separate 10 ml volumetric flask and volume was adjusted to the mark with methanol to get 9 μ g/ml of TELM and 9 μ g/ml of METO. Each solution was scanned between 200-400 nm against methanol as a reagent blank for zero order spectra (figure II). The second order derivative spectra of each solution was obtained using smoothing ($\Delta\lambda = 8$ nm) and scaling factor 20. The zero crossing points were found to be 224 nm and 299.5 nm for TELM and METO respectively (figure III). Wavelengths selected for quantification were 299.5 nm for TELM (zero crossing point for METO) and 224 nm for METO (zero crossing point for TELM).

Calibration curves for TELM and METO:

Standard TELM solutions of 3-15 μ g/ml were prepared by pipetting out 0.3, 0.6, 0.9, 1.2, and 1.5 ml of the working standard solution of TELM (100 μ g/ml) into series of 10 ml volumetric flasks and the volume was adjusted to mark with methanol. Absorbance of each solution was measured at 299.5nm using second order derivative spectrophotometry.A

calibration curve was prepared by plotting absorbance against respective concentration (Figure IV).

Standard METO solutions of 3-15 μ g/ml were prepared by pipetting out 0.3, 0.6, 0.9, 1.2 and 1.5ml of the working standard stock solution of METO (100 μ g/ml) into series of 10ml volumetric flasks and the volume was adjusted to mark with methanol. Absorbance of each solution was measured at 224 nm using second order derivative spectrophotometry. A calibration curve was obtained by plotting absorbance against respective concentration (Figure V).

Method validation¹⁵:

Linearity and range:

Aliquots of standard stock solutions of TELM and METO were taken in volumetric flasks and diluted with methanol to get final concentrations in range of 3-15 μ g/ml for both TELM and METO. This calibration range was prepared five times and absorbances were measured at respective wavelengths for each drug separately.

Precision:

Precision of the method was determined by performing interday variation, intraday variation and method repeatability studies. In interday precision, the absorbance of standard solutions of TELM (3-15 μ g/ml) and METO (3-15 μ g/ml) were measured on three consecutive days. In intraday variation the absorbances were measured three times in a day. For repeatability study, three concentration of both the drugs was measured three times.

Recovery studies:

To study the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different levels. A known amount of drug was added to pre analyzed sample powder and percentage recoveries were calculated.

LOD and LO:

For determination of LOD and LOQ calibration curve for both the drugs was repeated five times. The LOD & LOQ were calculated using mathematical equations given below.

$$\text{LOD} = 3.3 \times \sigma/S$$

$$\text{LOQ} = 10 \times \sigma/S$$

Where,

σ = Standard deviation of the Intercept

S = slope of calibration curve

Assay of tablet formulation:

Twenty tablets were weighed and crushed to obtain a fine powder. An accurately weighed tablet powder equivalent to about 50mg of TELM or 62.5 mg of METO was transferred to 50ml volumetric flask and the volume was made up to the mark using methanol. The solution was sonicated for 20 minutes. The solution was filtered through whatman Filter Paper No.42. First few ml of filtrate were discarded. 10ml of the above filtrate was diluted to 100 ml with methanol. 0.9 ml of above solution was further diluted to 10 ml with methanol. The absorbance of the resulting solution was measured using second order derivative spectrophotometry at 299.5 nm for TELM and 224 nm for METO. The concentration of each drug was calculated using equation of straight line.

RESULTS AND DISCUSSION

The proposed method was validated as per ICH guideline. The plot of absorbances versus respective concentrations of TELM and METO were found to be linear in the concentration range of 3-15 μ g/ml (Table I) and Figure IV, V. Interday variation, intraday variation and method repeatability studies were reported in term of co-efficient of variation (%C.V) (Table I). The %recovery ranges from 100.38-102.08% for TELM and 99.8-101.93% % for METO (Table I).

The derivative spectrophotometric method was applied to the estimation of TELM and METO in their combined dosage form (tablet). The results obtained indicate that the TELM and METO amounts found in the dosage form are comparable with the labeled amounts (Table II).

CONCLUSION

The proposed method was developed for the determination of TELM and METO in the presence of each other. Methods was validated and found to be simple, rapid, sensitive, specific, accurate, and precise. The method was successfully used to estimate the amounts of TELM and METO present in marketed tablet formulation containing TELM and METO.

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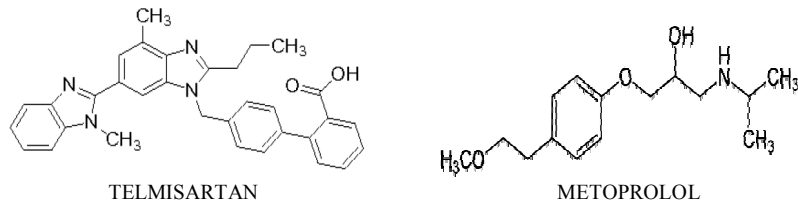


Figure I : Structure of Metoprolol and Telmisartan

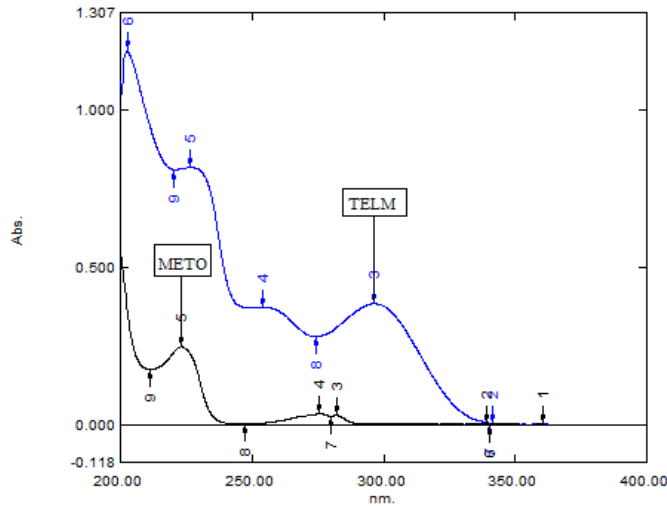


Figure.II: Overlain zero order spectra of TELM (9 µg/ml) and METO (9 µg/ml)

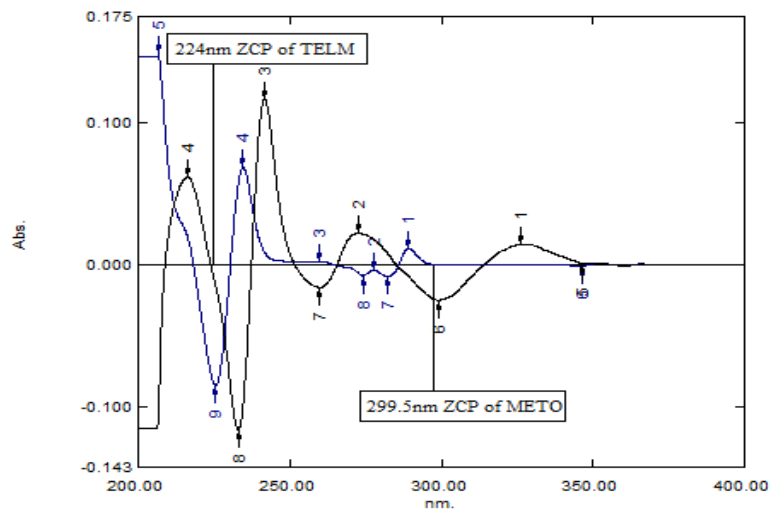


Figure III: Overlain second order derivative spectra of TELM (9 µg/ml) and METO (9 µg/ml):

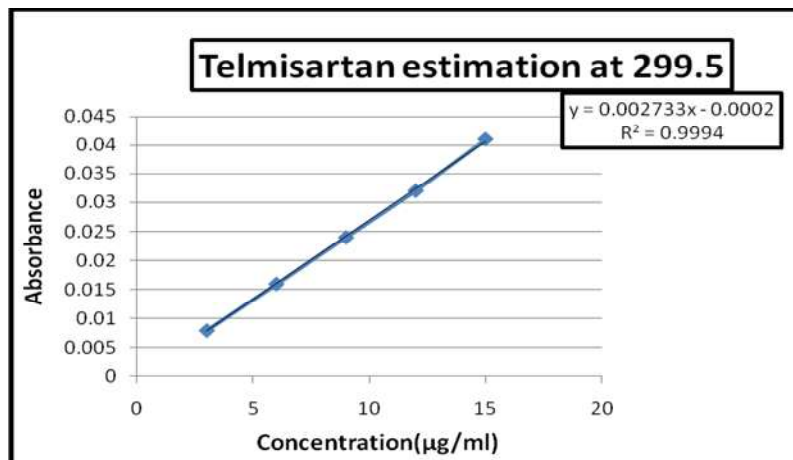


Figure IV: Calibration curve of standard TELM at 299.5 nm by second order derivative spectrophotometry.

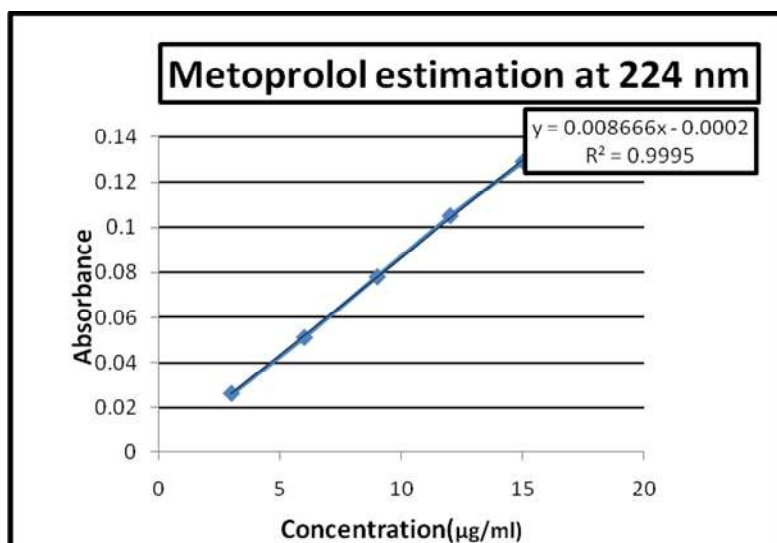


Figure V: Calibration curve of standard METO at 224 nm by second order derivative spectrophotometry.

Table I: Validation Parameters

Sr.No	Parameters	Result for TELM	Result for METO
1	Linearity Range (µg/ml)	3-15	3-15
2	Straight-line equation	Y=0.002733x-0.0002	Y=0.008666x-0.0002
3	Correlation coefficient (R ²)	0.9994	0.9995
4	Precision (% C.V.)		
	Repeatability(n=7)	1.56	0.68
	Intraday precision(n=3)	0.00-3.53	0.76-2.19
	Interday precision(n=3)	2.15-3.95	1.18-2.25
5	Accuracy (%recovery)	99.66-102.77	99.25-100.47
6	LOD (µg/ml)	0.47	0.14
7	LOQ (µg/ml)	1.45	0.44

Table II: Results of simultaneous estimation of TELM and METO in marketed Formulation.

Brand name	Company	Formulation	Labeled claim (mg)	% Labeled claim Found	
			TELM : METO	TELM	METO
TELSAR BETA 50	UNICHEM	Tablet	40 : 50	102.19%	100.31 %

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